Left fronto-parietal white matter correlates with individual differences in children's ability to solve additions and multiplications: a tractography study

Leen Van Beek[a], Pol Ghesquière[a], Lieven Lagae[b] & Bert De Smedt[a*]

[a] Parenting and Special Education, Faculty of Psychology and Educational Sciences, University of Leuven, Belgium

[b] Department of Development and Regeneration, Biomedical sciences group, University of Leuven, Belgium

Author e-mail addresses:

Leen Van Beek - Leen.VanBeek@ppw.kuleuven.be
Pol Ghesquière - Pol.Ghesquiere@ppw.kuleuven.be
Lieven Lagae - Lieven.Lagae@uzleuven.be
Bert De Smedt - Bert.DeSmedt@ppw.kuleuven.be

***Corresponding Author:**

Bert De Smedt
Faculty of Psychology and Educational Sciences
University of Leuven
Leopold Vanderkelenstraat 32 – box 3765
B-3000 Leuven
BELGIUM
Phone: + 32 16 32 57 05
Email: Bert.DeSmedt@ppw.kuleuven.be

Abstract

Functional neuroimaging data have pointed to the activation of a fronto-parietal network during calculation tasks, the activity of which is modulated by arithmetic operation and arithmetical competence. As the cortical brain regions of this network are distant, it is crucial to investigate the white matter connections between them and to examine how these connections are related to different arithmetic operations and individual differences in arithmetical competence. By using diffusion tensor imaging (DTI) tractography in eighteen 12-year-olds, we tested whether white matter pathways connecting these distant regions were related to children's arithmetical competence and how this association was modulated by operation. For each child, we delineated the three subcomponents of the arcuate fasciculus, a bundle of pathways linking frontal and temporo-parietal regions that are commonly active during calculation tasks. Fractional anisotropy in the left anterior portion of the arcuate fasciculus was positively correlated with addition and multiplication, but not with subtraction and division, suggesting a specific role of this left anterior segment in the solution of those problems that are expected to be solved with fact retrieval. The observed correlation was not explained by age, intelligence and working memory. Follow-up control analyses using different types of reading measures revealed that the observed correlation only disappeared when measures that draw heavily on phonological processing, such as non-word reading, were controlled for, suggesting that the association between the left arcuate fasciculus-anterior and addition/multiplication reflects the involvement of phonological processing. These results are the first to demonstrate that individual differences in fronto-parietal white matter are associated with arithmetical competence in typically developing children of a very narrow age range and indicate that this association is modulated by arithmetic operation.

Keywords : Diffusion Tensor Imaging (DTI), Tractography, Arcuate Fasciculus, Children, Arithmetic, Fact Retrieval

1. Introduction

Arithmetic is crucial in our daily life and represents an important part of the children's curriculum at school. At behavioral level large individual differences in learning arithmetic have been observed (Dowker, 2005). More recently, neuroimaging studies have started to unravel the neural correlates of these individual differences. Functional MRI studies in adults have revealed the activation of a fronto-parietal network during calculation tasks (Arsalidou and Taylor, 2011, for a review) and a similar fronto-parietal network has been observed in children (Kaufmann et al., 2011, for a review). Recent developmental fMRI data indicate that the activity in this network is modulated by arithmetic operation and individual differences in arithmetical competence (De Smedt et al., 2011). As the cortical brain regions of this network are distant, it is crucial to investigate the white matter connections between them and to examine how these connections are related to arithmetic operation and individual differences in arithmetical competence. Diffusion tensor imaging (DTI) is a powerful technique for studying these white matter connections and has been widely used to study brain-behavior relationships in children, particularly in the fields of reading (e.g., Beaulieu et al., 2005) and working memory (e.g., Nagy et al., 2004). DTI studies in arithmetic are scarce (but see Tsang et al., 2009; van Eimeren et al., 2008, 2010). To obtain more details about the neuro-anatomical correlates of arithmetic in children, the present study used DTI tractography to examine the association between fronto-parietal white matter and individual differences in children's arithmetical competence and how this association is modulated by operation.

Our specific attention to arithmetic is guided by different observations. First, arithmetic represents an important part of the children's curriculum at school and is a critical building block for subsequent mathematical skill development (Kilpatrick et al., 2001). By focusing on school-taught skills, such as arithmetic, the current study also adds to a growing body of data that include neural measures of school-taught performance, thereby contributing to the goals of the emerging field of Educational neuroscience (e.g., Goswami and Szucs, 2011). Second, a growing body of evidence points to deficits in arithmetic fact retrieval, or difficulties in direct retrieval of the answer from long-term memory, as a core deficit in children with mathematical learning disabilities or dyscalculia (e.g., Geary, 2004, 2010; Jordan et al., 2003). Lastly, most of the existing developmental behavioral (Geary, 2004, 2010; Jordan et al., 2003) and neuroimaging data (Arsalidou and Taylor, 2011; Kaufmann et al., 2011) about children's mathematical competence have focused on fact retrieval. As a consequence, the broad behavioral knowledge of arithmetic coupled with on the other hand, an understanding of the activation of the fronto-parietal network during arithmetic, have provided ground for the current structural neuro-imaging research about arithmetic.

Over the last two decades, the development of fMRI has greatly increased our knowledge about the brain regions involved in arithmetic. In adults, the ability to solve arithmetic problems relies on a network of both frontal and temporo-parietal brain areas (Ansari, 2008; Arsalidou and Taylor, 2011; Dehaene et al., 2003; Kaufmann et al. 2011; Menon et al., 2000a; Zamarian et al., 2009). The involvement of frontal areas does not appear to be specific to arithmetic processing. These frontal areas are believed to relate to executive functions and have mainly an auxiliary role in the maintenance of intermediate mental operations in working memory (Christoff and Gabrieli, 2000; Fehr et al., 2007; Owen et al., 2005). By contrast, parietal regions such as the bilateral intraparietal sulci (IPS), left angular and supra-marginal gyri, appear to be more specifically related to arithmetic processing. The IPS are found to be important for manipulation of quantity representations (Arsalidou and Taylor, 2011; Dehaene et al., 2003; Menon et al., 2000a). The more language related areas, including the left temporo-parietal cortex (including the angular gyrus, supra-marginal gyrus and posterior temporal cortex) and the left inferior frontal gyrus (IFG), are engaged during retrieval of verbally stored arithmetic facts (such as the multiplication tables) from long-term memory (Dehaene et al., 2003; Delazer et al., 2003; Prado et al., 2011; Rosenberg-Lee et al., 2011).

Adult fMRI data have shown that the activation in the abovementioned fronto-parietal network during arithmetic is modulated by operation (e.g., Fehr et al., 2007; Prado et al., 2011; Zhou et al., 2007). More specifically, fMRI data have demonstrated a dissociation between subtraction and multiplication. On the one hand, it has been shown that the IPS is more related to subtraction compared to multiplication (Chochon et al., 1999; Fehr et al., 2007; Kawashima et al., 2004; Lee, 2000; Piazza et al., 2007; Schmithorst and Brown, 2004; Simon et al., 2002). On the other hand, multiplication tasks have been shown to rely more on left temporo-parietal regions linked to verbal processing (Chochon et al., 1999; Delazer et al., 2003; Ischebeck et al., 2007; Jost et al., 2009; Lee, 2000; Prado et al., 2011; Schmithorst and Brown, 2004; Zhou et al., 2007). In line with all these findings in healthy adults, lesion studies with brain-injured patients suffering from difficulties in arithmetic have demonstrated a double dissociation between subtraction and multiplication. In particular, lesions in the left perisylvian cortex resulted in impairments in multiplication but not in subtraction, whereas lesions to regions of the intraparietal cortex were associated with difficulties with subtraction but not with multiplication (e.g., Cohen et al., 2000; Dehaene and Cohen, 1997).

The engagement of different neural networks for different operations likely reflects the use of different strategies (Barrouillet et al., 2008; Campbell and Xue, 2001; Chochon et al., 1999; Grabner et al., 2009; Imbo and Vandierendonck, 2008; Lee, 2000). Additions and multiplications are usually solved by means of highly automated calculation, such as fact retrieval. The left perisylvian cortex (i.e. angular and supra-marginal gyri) is a key region for retrieval of memorized facts from long-term memory (Grabner et al., 2009). Accordingly the left angular and supra-marginal gyri have been put forward as important underlying neural substrates for addition and multiplication (Chochon et al., 1999; Lee, 2000; Rickard et al., 2000). In contrast, subtractions and divisions are more often solved by more quantity-based procedural strategies with the engagement of IPS and the superior parietal lobe (Chochon et al., 1999, Kazui et al., 2000; Lee, 2000).

At behavioral level large individual differences in learning arithmetic have been observed (Dowker, 2005). More recently, neuroimaging studies have started to uncover the neural basis of these individual differences. Menon et al. (2000b) compared a group of perfect performers with a group of non-perfect performers on an arithmetic verification task with simple addition and subtraction. The authors found less activation within the left angular gyrus for perfect performers compared with non-perfect performers. In contrast, Grabner et al. (2007) found that adults of higher mathematical competence recruited to a greater extent the left angular gyrus during multiplication than less competent adults. These findings fit well with results of adult training studies, where young adults were trained for arithmetic problems and subsequently were compared for trained and untrained problems (Delazer et al., 2003, 2005; Grabner et al., 2009; Ischebeck et al., 2006, 2007, 2009). These studies found that increased proficiency with trained problems was associated with decreased activation in frontal areas and IPS and increased activity in the angular gyrus. On the one hand, these training studies show that expertise is associated with a greater involvement of inferior parietal areas (e.g., angular gyrus), which reflects a shift from effortful calculation to result retrieval from memory. On the other hand, expertise is linked to a decrease of activation within frontal brain areas, which reflects a diminished reliance on working memory and attentional resources.

Compared with the number of published studies investigating the neural correlates of arithmetic in healthy adults and patients, relatively few investigations have been performed with children. Moreover, data from studies of arithmetic processing in children have been less consistent. Most of the existing developmental studies have examined brain activation only during small additions. Available findings from these studies suggest that like adults children activate a fronto-parietal network during calculation tasks (Ansari et al., 2005; Ansari and Dhital, 2006; Davis et al., 2009; Kawashima et al., 2004; Kucian et al., 2008; Meintjes et al., 2010, for a recent review see Ashkenazi et al., 2013). Predominantly activations in prefrontal and inferior parietal brain regions have been observed. However, direct comparisons between adults and children revealed significant differences in the level of activations in frontal and parietal cortices. In particular, with experience and learning, there is decreased dependence on the prefrontal cortex and greater reliance on posterior parietal regions, including IPS (Ansari and Dhital, 2006; Cantlon et al., 2006; Davis et al., 2009; Kawashima et al., 2004). To the best of our knowledge, only one fMRI study specifically investigated the effect of arithmetic operation on brain activity in children (De Smedt et al., 2011). These authors examined the brain response to addition and subtraction in children aged 10–12 years. Commensurate with adult data, subtractions activated a fronto-parietal network, including IPS. Different from the adults, however, the left hippocampus rather than the (left) angular gyrus was more active during addition than during subtraction. The authors suggested that this region would especially be important in arithmetic for those problems that could be expected to be solved by fact retrieval, at least in the early stages of learning to retrieve arithmetic facts. This is in line with data by Cho et al. (2011, 2012), who investigated neurodevelopmental changes associated with increased use of fact retrieval strategies in 7- to 9-year-old children. They demonstrated that increased use of retrieval strategies in young children was associated with greater activation of prefrontal (i.e. left ventrolateral prefrontal and bilateral dorsolateral prefrontal cortex) and hippocampal regions. Consistent with this, Rivera et al. (2005) reported that the fronto-parietal arithmetic network in children is subject to age-related changes due to a strategy shift from effortful procedures to memory-based problem-solving with age. In particular, their developmental data provided evidence for an increased functional specialization of number-relevant areas (i.e. the left parietal cortex) in arithmetic along with an attenuation of activation in general-purpose areas (i.e. prefrontal areas) with age or growing expertise in arithmetic. These findings fit well with results of the abovementioned adult training studies, which showed that increased proficiency with trained problems was associated with decreased activation in frontal areas and IPS and increased activity in the angular gyrus .

Against the background of the studies reviewed above, it is clear that becoming skilled in arithmetic requires an adequate collaboration of the distant frontal and temporo-parietal regions involved in arithmetic. This implies an adequate communication between these cortical regions through white matter connections. DTI data have been used to identify and quantify these white matter connections and have become an important tool for relating individual differences in brain structure to cognitive functions, such as reading (Vandermosten et al., 2012b, for a review), working memory (e.g., Nagy et al., 2004) and (high-school) mathematics (e.g., Matejko et al., 2013). DTI is a MR technique which is sensitive to diffusion of water molecules in the brain (Basser et al., 1994; Beaulieu, 2002; Le Bihan et al., 2001; Mukherjee et al., 2008). In grey matter and cerebrospinal fluid, diffusion occurs almost equally in all directions due to few boundaries. These tissues, where diffusion is more a random process, are called isotropic. In contrast, white matter can be considered to be highly anisotropic because water has strong directional dependence due to the presence of myelin sheaths and cell membranes. In particular, diffusion across the axon is significantly smaller than diffusion along the axon. This anisotropy is exploited in DTI to get insight in the white matter microstructural anatomy of the brain. The measurement of fractional anisotropy (FA), an index of the degree of directionality of diffusion that is determined by both microscopic factors, such as myelination (Mori, 2007) and macroscopic factors, such as crossing fibers, is commonly used and has been successful in identifying the neuro-anatomical correlates of cognitive functions, such as working memory (e.g., Olesen et al., 2003), intelligence (e.g., Schmithorst et al., 2005) and reading (Vandermosten et al., 2012b, for a review).

Previous developmental DTI research in the field of mathematics learning has primarily focused on the association between mathematics and diffusion parameters in atypical populations, such as dyscalculia (Rykhlevskaia et al., 2009), fetal alcohol spectrum disorder (Lebel et al., 2010), and velocardiofacial syndrome (Barnea-Goraly et al., 2005). These studies suggest that individual differences in numerical and mathematical performance may be related to left frontal and parietal white matter structures and specific white matter tracts connecting these regions, e.g., white matter adjacent to the left IPS, supramarginal and angular gyri, the left superior longitudinal fasciculus, left corticospinal tract and corpus callosum (Barnea-Goraly et al., 2005; Lebel et al., 2010; Rykhlevskaia et al., 2009). However, some studies demonstrated that white matter in the right hemisphere might be involved in mathematics as well. For example, Rykhlevskaia et al. (2009) investigated a sample of children with developmental dyscalculia and observed deficits in right hemisphere temporo-parietal white matter and pathways associated with it, including the inferior fronto-occipital fasciculus and the inferior longitudinal fasciculus. Likewise, Till et al. (2011) found significant correlations between calculation scores and white matter in right frontal and parietal regions in multiple sclerosis patients.

Overall, there is some developmental evidence from atypically developing children to suggest that left frontal and parietal white matter structures are important for numerical and mathematical processing. Additionally, DTI data from healthy adolescents and adults have also significantly added to our understanding of the underlying neural correlates of mathematics. Van Eimeren et al. (2010) combined DTI and fMRI data while adult participants performed a mental arithmetic task. They found a correlation between white matter integrity in the left temporo-parietal cortex (i.e. left superior corona radiata) and activity of the left angular gyrus, which was particularly strong during problems that have a high probability of being solved by arithmetic fact retrieval. More recently, Matejko et al. (2013) observed in 17-18-year-old adolescents a significant association between left parietal white matter and individual differences in the math scores of the Preliminary Scholastic Aptitude Test, a college entry exam, and this association remained when age and reading scores were controlled for. Although these studies in healthy adolescents and adults provided evidence for the involvement of a structural fronto-parietal white matter network in mathematics, these findings cannot be readily generalized to typically developing children.

To date, little is known about the relationship between white matter and arithmetical competence in typically developing children, with only two DTI studies published. Van Eimeren et al. (2008) found correlations between FA in left temporo-parietal regions, such as the superior corona radiata and left inferior longitudinal fasciculus, with children's written arithmetical ability. Tsang et al. (2009) used DTI tractography in typically developing children (10-15 years) to examine the association between white matter and arithmetical skills. Up to now, this study of Tsang et al. (2009) is the only tractography study in research on mathematical learning. DTI tractography has the unique ability to delineate in vivo specific white matter pathways between distant cortical brain regions, such as the frontal and temporo-parietal regions that are active during arithmetic. The main advantage of region of interest (ROI) based tractography, as used by Tsang et al. (2009), lies in its high sensitivity to subtle differences (for a description of strengths and weaknesses of different DTI-methods see Cercignani, 2010). Compared to tract-based spatial statistics (TBSS), which has been introduced to overcome accuracy problems of voxel-based analysis due to imperfect registration and smoothing, tractography has the advantage of extending the analysis to the entire tract volumes, and not only to the central skeleton line. This allows a more comprehensive evaluation of white matter tracts. However, for a reliable and reproducible positioning of ROIs, knowledge of basic anatomy and definition of clear guidelines is required. These are not numerous, but some published guidelines do exist (Catani and de Schotten, 2008; Wakana et al., 2007). Moreover, ROI-based tractography requires a strong a priori hypothesis about the location of interest. In spite of these disadvantages, ROI- based tractography is recommended when the researcher is interested in small differences in well-defined brain areas.

Tsang et al. (2009) found that FA of the left arcuate fasciculus-anterior, referred to these authors as the anterior superior longitudinal fasciculus, was correlated with approximate addition, but not with approximate multiplication, exact addition or written math ability. However, Tsang et al. (2009) sampled children of a broad age range, i.e. 10-15 years. Although the authors controlled for age in their analysis, it is not clear whether the same findings can be replicated in a group children of a more narrow age. Moreover, Tsang et al. (2009) mainly focused on addition. However, the fMRI studies in both adults and children reviewed above indicated that the arithmetic fronto-parietal network is modulated by operation. Given that the four basic arithmetic operations rely on different strategies and are associated with the engagement of different neural networks, differences between numerical operations can be expected. Against this background, this study is set out to investigate whether correlations between fronto-parietal white matter and arithmetical competence diverge as function of operation.

The present study

To address these outstanding questions, we aimed to extend the current understanding of the neuro-anatomical correlates of arithmetic in children by conducting a DTI tractography study. In particular, we wanted to examine the association between individual differences in mathematics achievement and the quality of the white matter pathways that connect frontal and temporo-parietal regions that are active during arithmetic. Against the background of fMRI studies that show that this arithmetic network is modulated by operation, we further aimed to verify whether the abovementioned association was modulated by the type of operation. The bundle of white matter pathways with projections to frontal, parietal, and temporal lobes, has been referred to as the arcuate fasciculus (Catani et al., 2005) or the superior longitudinal fasciculus (Oishi et al., 2011; Wakana et al., 2007) (see Dick and Tremblay (2012), who reviewed the consensus and controversy in the definitions of the superior longitudinal fasciculus and arcuate fasciculus). Catani et al. (2005) demonstrated that the arcuate fasciculus consists of three distinct segments: (i) a long segment connecting frontal and temporal lobes located medially (arcuate fasciculus – direct, AFdirect); (ii) an anterior lateral segment connecting frontal and inferior parietal cortex (arcuate fasciculus – anterior, AFanterior); and (iii) a posterior lateral segment connecting temporal and inferior parietal cortex (arcuate fasciculus – posterior, AFposterior). These three separate segments may be differentially related to different arithmetic operations. Therefore, in line with Catani et al. (2005) we will use the term arcuate fasciculus and its subdivision to refer to this bundle of pathways connecting frontal, parietal and temporal areas that are often active during calculation tasks. In fact, there are three main reasons why we focus on the arcuate fasciculus. First, this bundle connects different important components of the arithmetic network. Second, to the best of our knowledge only one study (Tsang et al., 2009) in arithmetic explicitly delineated the arcuate fasciculus using tractography. The current study builds on these data but further extends this study by examining in a more narrow age range how the three subcomponents of the arcuate fasciculus relate to different arithmetical operations. As mentioned earlier, it is important to structurally subdivide the arcuate fasciculus into its three components because each of them may yield distinct functions. However, Tsang et al. (2009) only delineated the arcuate fasciculus-anterior, which these authors denoted by the anterior superior longitudinal fasciculus, as tract of interest and the arcuate fasciculus-direct, which these authors referred to as the arcuate fasciculus, as control tract. Third, the role of the arcuate fasciculus in reading, especially in initial stages of reading, or phonological decoding, such as reading of unfamiliar words or non-words, is well documented (Vandermosten et al., 2012a; Yeatman et al., 2011). Also imaging data have pointed to the activation of a left fronto-temporo-parietal network during reading tasks, especially when appealing to phonological skills, i.e. during reading of unfamiliar letter strings, such as non-words, and at the initial stages of reading development (Cohen et al., 2008; Pugh et al., 2000; Simos et al., 2002). Finally, neuroimaging studies have shown a neural overlap between reading and arithmetic in the left temporo-parietal cortex (Dehaene et al., 2003; Pugh et al., 2001) and it has been suggested that some arithmetic operations, such as multiplication, might require phonological processing (e.g. Dehaene et al. 2003). In light of this, it is important to examine the role of the arcuate fasciculus in arithmetic.

In the present study, we delineated according to validated protocols (Catani et al., 2005; Catani and de Schotten, 2008; Wakana et al., 2007) the three segments of the arcuate fasciculus in both the left and right hemisphere in typically developing 12-year-olds. FA values were extracted and correlated with measures of children’s arithmetical achievement scores which varied as function of arithmetic operation, i.e. addition, multiplication, subtraction and division scores. The specificity of the findings was further investigated by including age, intelligence and working memory as covariates in the analyses. Given that the four basic arithmetic operations are associated with the engagement of different neural networks, we expected differences between numerical operations. More precisely, based on previous literature that the arcuate fasciculus projects to the inferior parietal cortex (e.g., angular and supra-marginal gyri) and posterior parts of the superior and middle temporal gyrus, and not to superior parietal cortex (e.g., IPS), we hypothesized that white matter in the arcuate fasciculus would be related to addition and multiplication, but not to subtraction and division scores.

Because the left arcuate fasciculus and temporo-parietal cortex are implicated in reading ability, we also investigated whether the observed pattern of findings remained when reading ability was additionally controlled for. To this end, we administered two measures of reading ability, i.e. a test of word reading (Brus and Voeten, 1979) and a test of pseudo-word reading (van den Bos et al., 1994). The distinction between the two reading tests is particularly relevant because it has been proposed that reading is subserved by two distinct neural circuits (in the left hemisphere) that are related to the use of different reading strategies: (i) a ventral orthographic route, which is related to the direct recognition of words and (ii) a dorsal phonological route, which involves the grapheme-to-phoneme mapping or phonological decoding (Jobard et al., 2003; Sandak et al., 2004; Schlaggar and McCandliss, 2007). The ventral orthographic route, situated in the left ventral occipito-temporal cortex near the fusiform gyrus, is recruited for visual word processing, i.e. when the visual input is directly decoded , a route that is used for reading familiar words (Cohen et al., 2008; Pugh et al., 2000; Sandak et al., 2004; Simos et al., 2002). By contrast, the phonological route taps more in to phonological processing because the graphemes of a word need to be mapped (one-by-one) onto phonemes. This route involves the recruitment of left fronto-parietal networks and is typically required for reading unfamiliar letter strings, such as nonwords, and at the initial stages of reading development (Cohen et al., 2008; Pugh et al., 2000; Simos et al., 2002). Against this background, we selected two reading tests, one that relied more on visual word processing, i.e. the word decoding test, and one that relied more on phonological processing, i.e. the pseudo-word reading test. Including the two reading tests allowed us to verify whether the observed association could be explained by reading ability in general or more specifically by phonological processing.

2. Methods

2.1. Participants

Twenty-five typically developing children participated in this study. Due to excessive movement artefacts (*n* = 2), technical acquisition problems (*n* = 1), claustrophobia (*n* = 1) and left-handedness (*n* = 3) we had to exclude seven children from the analyses. The final sample consisted of 18 children (*M* = 12.0 years; *SD* = 0.4; age range 11.5 – 12.9 years; 8 boys). All included participants were healthy, native Dutch speakers, predominantly right-handed as assessed by the Edinburgh Handedness

Inventory (Oldfield, 1971). They all had normal intelligence (IQ > 85; *M* = 108; *SD* = 12) as determined by an abbreviated version of the Dutch Wechsler Intelligence Scale for Children, Third Edition (WISC-III-NL; Kort et al., 2005). All children had normal or corrected-to-normal vision. The parents of the children did not report any history of neurologic problems, psychiatric disorders or learning difficulties. Children were recruited from schools in and around Leuven, Belgium. The study was approved by the local Ethical Board and written informed consent according to the Declaration of Helsinki was obtained from the children as well as their parents. We initially explored whether there were any gender differences in the current data. There were no differences between boys and girls for all variables under study (all *p*s > .061).

2.2. Behavioral measures

2.2.1. Arithmetical competence

Arithmetical competence was measured by the Tempo Test Arithmetic (De Vos, 1992). This standardized paper-and-pencil achievement test consists of several subtests that require elementary computations. Each subtest involves only one arithmetic operation, i.e. addition, subtraction, multiplication or division, and consists of 40 items of increasing difficulty. The child was given one minute for each subtest and had to solve as many problems as possible within that minute. Performance on each subtest was the total of the correctly solved problems for that operation. The maximum score for each subtest was 40.

2.2.2. Intellectual ability

Children were assessed with an abbreviated version of the Dutch Wechsler Intelligence Scale for Children, Third Edition (WISC-III-NL; Kort et al., 2005) to estimate their IQ. The Vocabulary and Block Design subtests were administered and the scores on these subtests were combined into a full scale IQ (Sattler, 2001).

2.2.3. Working memory

Visuo-spatial and verbal-auditory working memory were assessed by four different tasks that are commonly used in research in children (e.g., De Smedt et al., 2009; Gathercole et al., 2004). These tasks were drawn from the Working Memory Test Battery for Children (Pickering and Gathercole, 2001). Visuo-spatial working memory was assessed by forward and backward Block Recall, whereas verbal-auditory working memory was assessed by forward and backward Digit Recall. In each of the working memory tasks the child was asked to repeat a sequence of test items to the researcher. In the forward tasks children had to repeat items in the same order as presented, whereas in the backward tasks children had to produce the items in the reverse order as presented. In the Digit Recall tasks sequences of random digits were presented verbally and the child was asked to verbally repeat them in either the same or reverse order as presented. In the Block Recall task a set of identical blocks were placed between the researcher and child, with the former tapping the blocks in sequences that the child was required to copy in either the same or reverse order. For each task blocks of three trials of a particular sequence length were used. If a child made two errors in a block the task was ended. The score of each working memory task was based on the total number of correct trials that could be recalled by the child. The total working memory score, i.e. the sum of scores on the four tasks was used as covariate in the correlation analyses.

2.3. Reading ability

Two tests for reading, i.e. a word (Brus and Voeten, 1979) and pseudo-word reading test (Van den Bos et al., 1994), were administered. Both tests required the speeded reading of lists of words/pseudo-words of increasing difficulty. The score on the word reading test was the number of real words read correctly in one minute, whereas the score on the pseudo-word reading test was the number of pseudo-words read correctly in two minutes. It should be noted that these reading data were collected 15 months after other behavioral and DTI data. While this might be a potential limitation to our study, this gap in time probably not affects our findings because scores on the two reading tests do not change dramatically within one year after the age of 12 (Van den Bos et al., 1994).

2.4. DTI acquisition and analysis

All participants underwent MRI examination on a 3T system (Philips Achieva, Best, The Netherlands). The DTI data were acquired using a single spin shot EPI with SENSE acquisition. DTI images covering the entire brain and brainstem were acquired with the following parameters: 68 contiguous sagittal slices, slice thickness = 2.2 mm, voxel size = $1.96 \times 1.96 \times 2.2$ mm^3, repetition time (TR) = 11043 ms, echo time (TE) = 55 ms, field-of-view (FOV) = 220×220 mm^2, matrix size = 112×109 and acquisition time = 10 min 34 s. Diffusion gradients were applied along 45 non-collinear directions (b = 800 s/mm^2) and one nondiffusion-weighted image was acquired.

Raw diffusion MR data were transferred to an offline workstation. All images were first visually checked for possible artifacts and participants whose images were of poor quality were removed (n = 2). Further preprocessing was done using *ExploreDTI* (Leemans et al., 2009). The preprocessing involved (i) correcting for eddy current distortion and subject motion; (ii) diffusion tensor estimation using a non-linear least square method, and (iii) whole brain tractography for each DTI data set using a uniform 2 mm seed point resolution, FA threshold of .2 to seed and end tracking, angle threshold of 40°, and fiber length range of 50-500 mm.

Tractography was done with the TrackVis software (Wang and Wedeen, 2007). We delineated the tracts of interest in native space in order to avoid artifacts due to normalization. As mentioned in the introduction, the three segments of the arcuate fasciculus were reconstructed. To reconstruct these tracts, we defined the ROIs according to the available validated protocols for delineation of the arcuate fasciculus (see Fig. 1; Catani et al., 2005; Catani and de Schotten, 2008; Wakana et al., 2007). This approach has been applied successfully in previous research (Vandermosten et al., 2012a). In line with Catani et al. (2005), we subdivided the arcuate fasciculus in three distinct segments: (i) AFdirect (red fibers in Fig. 1); (ii) AFanterior (green fibers in Fig. 1); and (iii) AFposterior (yellow fibers in Fig. 1). The three segments of the arcuate fasciculus were delineated both in the left and right hemispheres. We were able to delineate the three segments of the arcuate fasciculus in all children, except for the right AFdirect, which was only found in 11 of the 18 subjects (61%). This is consistent with previous studies (Catani et al., 2007). For each of the tracts the FA values were extracted for every subject. To assess the reproducibility of the tractography, the delineation of the arcuate fasciculus was performed by two independent and experienced raters. We observed high inter-rater reliability as indicated by a FA intra-class correlation coefficient >.94. Against this background, the average FA across the two raters was used in all subsequent analyses. In order to take into account individual differences in the estimation of the diffusion tensor, we calculated an index of goodness of tensor estimation fit and included it as a covariate in the correlational analyses. This index represents the mean residual of all the diffusion weighted images, i.e. absolute residual value to the tensor fit (the lower the value, the better the fit). Thus by including this value (mean chi-square) as a covariate, we take into account subtle noise differences between subjects, which may influence the tensor fitting and eventually the FA value. In the manual of *ExploreDTI* (Leemans et al., 2009) this metric is part of the standard protocol to assess the quality of the DTI-data. Several other DTI-researchers have also applied this metric, which can be considered to indicate the quality of DTI data acquisition, as a covariate in their correlational analyses (e.g., Deprez et al., 2012; Vandermosten et al., 2012).

In the initial analysis, scores on the arithmetical achievement test were correlated with the extracted mean FA values of each tract. Secondly, partial correlations that additionally controlled for the effects of chronological age, intelligence, and working memory were run between the arithmetic scores and the extracted FA values. This was done to reduce the likelihood that the observed associations between FA values and arithmetic were explained by age or domain-general cognitive skills. Finally, we verified whether the observed correlations remained or disappeared, when different types of reading ability were additionally taken into account. In all correlational analyses, Bonferroni adjustments were made to account for multiple comparisons.

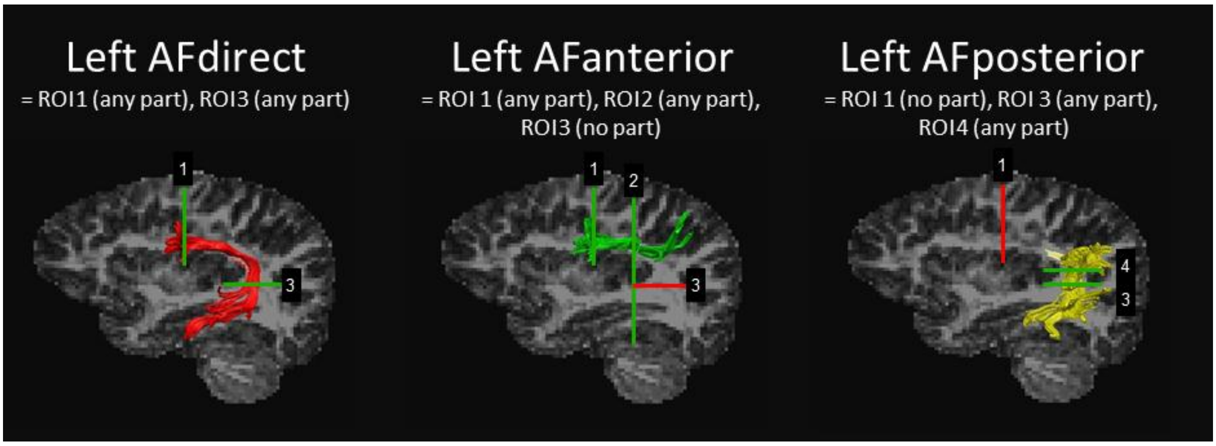

Fig. 1. TrackVis example of fibertracking of the three subcomponents of the arcuate fasciculus (AF) in one subject in native space on sagittal fractional anisotropy data.

3. Results

The performance scores on the four subtests of the arithmetical achievement test were: addition (*M* = 31, *SD* = 3, range 25 - 34), subtraction (*M* = 28, *SD* = 3, range 24 - 32), multiplication (*M* = 27, *SD* = 4, range 19 - 32) and division (*M* = 27, *SD* = 3, range 20 - 33). No ceiling effects occurred as none of the children answered all 40 problems for a given operation within the time limit. Descriptive statistics on fractional anisotropy are displayed in Table 1.

Table 1. Fractional anisotropy (FA) of the three subcomponents of the arcuate fasciculus (AF)

	M (SD)
Left AFdirect	.517 (.026)
Left AFanterior	.476 (.026)
Left AFposterior	.488 (.022)
Right AFdirect	.481 (.031)
Right AFanterior	.474 (.028)
Right AFposterior	.478 (.022)

For the correlation of FA with arithmetical competence, Pearson correlations between FA values of the different tracts and arithmetic scores were calculated. Significant associations between FA in the left arcuate fasciculus-anterior and addition and multiplication were found, indicating that larger FA values were associated with better arithmetical performance (see Table 2 and Fig. 2). Subtraction and division were not significantly correlated with FA in the left arcuate fasciculus-anterior. There were no significant associations between FA values in the direct or posterior part of the arcuate fasciculus and arithmetical competence.

Table 2. Pearson partial correlations (controlled for quality index of DTI acquisition) between mean FA and arithmetical competence

		Arithmetical competence			
		Addition	Subtraction	Multiplication	Division
Left AF	Direct	.409	-.011	.470	.202
	Anterior	.704**	.219	.722**	.353
	Posterior	.294	-.076	.269	-.144
Right AF	Direct	.166	-.155	.191	.185
	Anterior	.395	.215	.384	.143
	Posterior	.259	-.185	.303	.097

** Bonferroni corrected $p < .01$; AF = arcuate fasciculus

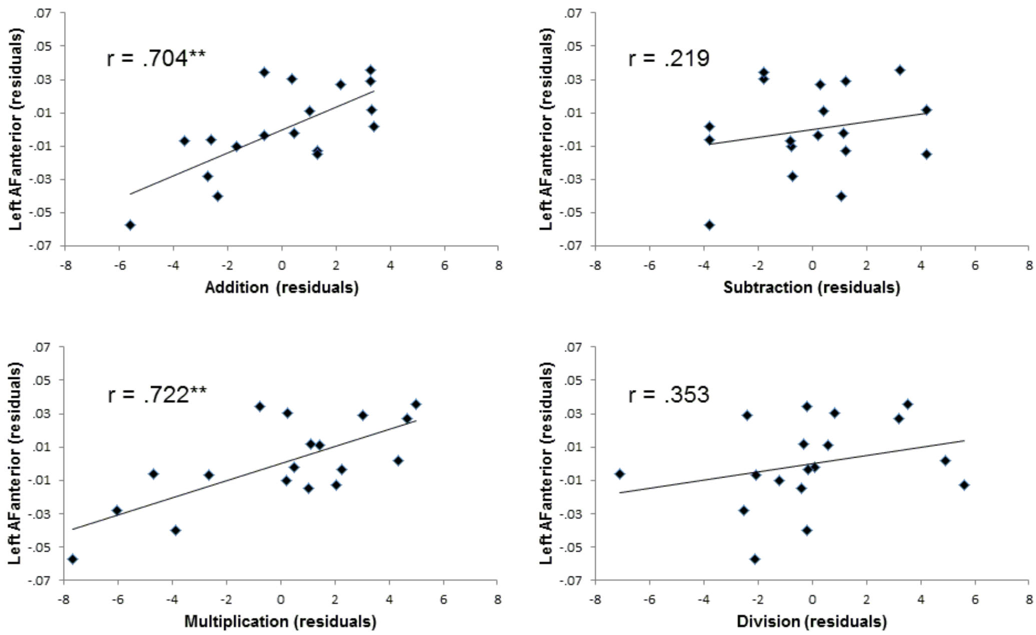

Fig. 2. Correlations between (residual) FA value of the arcuate fasciculus-anterior (AFanterior) and (residual) arithmetical competence after controlling for quality index of DTI acquisition. The solid line represents the linear regression for this relationship. Correlations for addition and multiplication were significant ($p < .01$, Bonferonni corrected), whereas the associations for subtraction and division were not significant (ps > .268).

We further evaluated whether the observed significant correlations for addition and multiplication were not just an effect of task difficulty or subtest differences in arithmetical performance. A one-way ANOVA with operation as within-subject factor revealed that the average performance differed between the four subtests ($F(3,68) = 6.026$; $p < .01$). Post-hoc comparisons using the Tukey HSD test indicated that only addition was significantly different from multiplication ($p = .001$) and division

(p = .005), but from subtraction (p = .064). The multiplication score did not significantly differ from subtraction (p = .554) or division (p = .983). These analyses indicate that while there were significant differences as function of task, the scores on the subtests correlated with FA, i.e. addition and multiplication, were not significantly higher than those on subtests that were not correlated with FA, i.e. subtraction and division. This all indicates that the observed correlations are not merely explained by recourse to task difficulty.

We also investigated the specificity of the observed correlations between the arcuate fasciculus-anterior and addition/multiplication by applying statistical comparisons of the observed correlations in Table 2. This was done by using the William-Steiger test for comparing correlations within a population. Firstly, we explored whether the correlations between left arcuate fasciculus-anterior and the different operations were significantly different from one another. These analyses revealed that the significant correlations for addition and multiplication were significantly larger than the (non-significant) correlations observed for subtraction and division (all ts > 2.647, all ps < .019). This all indicates that the association between arithmetic and FA in the left arcuate fasciculus-anterior seems to be specific for addition and multiplication. Secondly, we also checked whether the observed significant correlations between addition/multiplication and the left arcuate fasciculus-anterior were specific for the left hemisphere. Again, we performed a William-Steiger test and this test revealed that the significant correlations on the left hemisphere were statistically different from all non-significant correlations in the right hemisphere (all ts > 2.210, all ps < .043). Finally, we also verified whether significant correlations in the anterior part were statistically different from the remaining non-significant correlations in other subcomponents of the arcuate fasciculus. William-Steiger tests revealed that the observed significant correlations for addition/multiplication in the left arcuate fasciculus-anterior were indeed statistically different from the non-significant correlations in the direct and posterior part of the arcuate fasciculus (all ts > 2.210, all ps < .043), except for the left arcuate fasciculus-direct-addition correlation which was only marginally different from the left arcuate fasciculus-anterior-addition correlation (t = 1.830, p = .087). Overall these results indicate that the observed correlations between addition/multiplication and the left arcuate fasciculus-anterior are significantly different from the associations with subtraction/division. These data also indicate that this pattern of findings is not observed in the right hemisphere or adjacent subcomponents of the arcuate fasciculus. In other words, these findings demonstrate the anatomical specificity of the arithmetic correlation found in the left arcuate fasciculus-anterior.

Because the observed associations could be due to differences in general cognitive abilities, we tested the possibility that the observed correlations were explained by shared variance between addition/multiplication and other cognitive abilities, such as intelligence and working memory, or age. When additionally controlled for age, IQ and working memory the observed correlations between FA in the arcuate fasciculus-anterior and addition ($r = .721$, Bonferroni corrected $p = .004$) and multiplication ($r = .746$, Bonferroni corrected $p = .002$) remained significant. Also, the abovementioned comparisons of correlations to test for the anatomical specificity of the observed correlations with arithmetic in the left arcuate fasciculus-anterior remained the same when age, IQ and working memory were additionally controlled for.

Finally, we investigated whether the observed relationship between the left arcuate fasciculus-anterior and addition/multiplication could be explained by differences in reading abilities. This was done by controlling the correlation between FA in the left arcuate fasciculus-anterior and addition and multiplication for both measures of reading ability separately. Interestingly, the observed correlations between FA of the arcuate fasciculus-anterior and addition ($r = .711$, Bonferroni corrected $p < .01$) and multiplication ($r = .734$, Bonferroni corrected $p < .01$) remained significant when additionally controlled for word reading. However, when pseudo-word reading was taken into account, the observed correlations for addition ($r = .469$, $p > .05$) and multiplication ($r = .526$, $p > .05$) disappeared. These data suggest that the observed associations between left arcuate fasciculus-anterior and addition/multiplication, might be explained by the common involvement of phonological processes.

4. Discussion

We used DTI tractography in a sample of typically developing children of a very narrow age range to evaluate the hypothesis that individual differences in children's arithmetical competence are associated with white matter pathways connecting regions of the fronto-parietal arithmetic network, and explored how this association is modulated by arithmetic operation. More specifically, we investigated which of the four basic arithmetic operations (i.e. addition, multiplication, subtraction and division) was associated with fractional anisotropy of the arcuate fasciculus, subdivided into its three subcomponents (i.e. direct, anterior and posterior part). Our results showed a link between fractional anisotropy of the left anterior part of the arcuate fasciculus, which directly connects frontal and inferior parietal areas, and individual differences in children's arithmetical competence. This association was specifically observed for addition and multiplication, but not for subtraction and division.

Over the last decades, converging evidence has identified a fronto-parietal network during arithmetic, comprising distant frontal and temporo-parietal regions (Ansari, 2008; Arsalidou and Taylor, 2011; Zamarian et al., 2009). In addition to the growing body of functional neuroimaging studies underlying arithmetic, there is an increasing interest in investigating underlying white matter structures that connect the different areas of this arithmetic network (Tsang et al., 2009; van Eimeren et al., 2010). We used DTI tractography to further unravel specific neuroanatomical correlates of arithmetic. Based on functional neuroimaging data and previous DTI findings, we had a strong a priori hypothesis about the location of interest, i.e. the arcuate fasciculus, a bundle of pathways connecting frontal, parietal and temporal regions of the arithmetic network. DTI tractography is often avoided due to lack of knowledge about basic anatomy or clear guidelines for delineation of the tracts of interest. However, for delineation of the arcuate fasciculus published guidelines with validated protocols do exist (Catani et al., 2005; Catani and de Schotten, 2008; Wakana et al., 2007). Current DTI tractography methods require the delineation of ROIs as starting 'seed points' for tracking (Jones, 2008). We defined our ROIs manually based on the aforementioned available guidelines for the arcuate fasciculus (Catani et al., 2005; Catani and de Schotten, 2008; Wakana et al., 2007).

What can be inferred from the results? First, we demonstrated that fronto-parietal white matter is strongly related to individual differences in children's arithmetical competence. This finding is consistent with previous DTI studies in mathematics, which predominantly observed associations between mathematics and diffusion parameters in frontal and parietal regions (Barnea-Goraly et al., 2005; Matejko et al., 2013; Lebel et al., 2010; Rykhlevskaia et al., 2009; Till et al., 2011; Tsang et al., 2009; van Eimeren et al., 2010). The present results demonstrate that the brain-behavior relationships observed in these previous studies are not restricted to atypically developing children (Barnea-Goraly et al., 2005; Lebel et al., 2010; Rykhlevskaia et al., 2009; Till et al., 2011), children of a broad age range (Tsang et al., 2009; van Eimeren et al., 2010) or adults (Matejko et al., 2013), but remain evident in typically developing 12-year-olds. Similar to Tsang et al. (2009), who also used tractography, we found a relationship between fractional anisotropy of the arcuate fasciculus-anterior and arithmetic. However Tsang et al. (2009) only found a correlation with approximate addition and failed to find any correlations between the arcuate fasciculus-anterior and measures of exact arithmetic. By contrast, the findings of the present study revealed a correlation between the arcuate fasciculus-anterior and exact arithmetic. It is important to note that the methods used in both studies differed in several ways, which may have led to conflicting data about exact arithmetic. First, it is important to emphasize that both studies used different types of tasks to measure exact arithmetic. Tsang et al. (2009) administered verification tasks, whereas the present study used production tasks. As a consequence children in both studies may have solved the arithmetic problems by different strategies. For example, in Tsang et al. (2009) children may have used parity-checking or plausibility-checking solving strategies rather than explicitly calculating or retrieving the solution. Moreover, the tasks used by Tsang et al. (2009) were untimed. Children in their study received six seconds for each item, which is a relatively large amount of time for such easy problems. Also, in Tsang et al. children were allowed to solve all the available problems, whereas in the current study, the number of problems solved within the time limit. So, even though in both studies the outcome was the number of correctly solved items, the outcome in the present study relied much more on a combination of accuracy and reaction time, whereas the outcome of Tsang et al. was far less (or even not) dependent on the speed at which children solve the arithmetic problems. Furthermore, the age range differed in both studies. Tsang et al. tested children of a broad age range, whereas we chose to select only a specific age, i.e. 12-year-olds. This was done to exclude as much as possible potential age-related differences and to ensure that the children in the current study were as homogenous as possible in terms of the amount of received mathematics instruction. We focused on 12-year-olds because at this age we expected them to have already required a substantial degree in automatization in arithmetic fact retrieval. Finally, we looked whether the whole arcuate fasciculus-anterior was correlated with arithmetic, whereas Tsang et al. only selected a central chunk of this tract of interest. Taken together all these elements may explain the disparities between the current findings and those of Tsang et al. (2009).

Secondly, it is important to point out that the observed relationship between white matter and arithmetic is not explained by age, intelligence and working memory. Since the anterior part of the arcuate fasciculus has frontal terminations, the relationship we observed could be due to general cognitive abilities which rely on frontal brain regions, such as working memory. This was not the case.

Third, the observed relationship between fronto-parietal white matter and children's arithmetical competence appears to be modulated by arithmetic operation. In terms of operation, we found that fractional anisotropy of the left anterior part of the arcuate fasciculus correlated with addition and multiplication, but not with subtraction and division. Moreover, the correlations for addition and multiplication were significantly larger than the (non-significant) correlations observed for subtraction and division. This further supports this idea of operation specificity of the correlation between the arcuate fasciculus-anterior and addition/multiplication. These findings data are highly congruent with functional neuroimaging studies in typically developing children (De Smedt et al., 2011), healthy adults (Fehr et al., 2007; Prado et al., 2011; Zhou et al., 2007) and brain-injured patients (e.g., Cohen et al., 2000; Dehaene and Cohen, 1997), which have shown a dissociation among simple arithmetic operations. Although the activation in the fronto-parietal arithmetic network is modulated by operation, none of the previous DTI studies in mathematics looked into differences between arithmetic operations. Thus, our study extends earlier research by exploring this difference. In particular, we add new information to the DTI tractography findings of Tsang et al. (2009) by showing that structural properties of left fronto-parietal pathways are correlated with arithmetic abilities, but that this is modulated by arithmetic operation. Based on our results, the arcuate fasciculus-anterior is proposed as anatomical correlate for addition and multiplication, but not for subtraction and division.

Fourth, the observed dissociation between arithmetic operations might reflect the use of different strategies. Behavioral studies in typically developing children have shown that different arithmetic operations are solved by different strategies, i.e. arithmetic fact retrieval and, on the other hand, procedural strategies, such as counting or decomposing a problem into smaller problems (Barrouillet et al. 2008; Imbo and Vandierendonck, 2008; Siegler, 1996). More specifically, addition and multiplication are mainly solved by fact retrieval, already from second grade on (Imbo and Vandierendonck, 2008). In contrast subtractions are more often solved by procedural strategies, which are assumed to rely on quantity-based processes (Barrouillet et al., 2008). The observed dissociation between arithmetic operations in the current study might reflect the use of different strategies, i.e. fact retrieval for addition and multiplication versus more quantity-based procedural strategies for subtraction and division. This is in line with Dehaene's triple code model (Dehaene, 1992; Dehaene et al., 2003) which postulates that answers to retrieval-based operations, such as simple addition and multiplication, are stored in verbal memory, located in the left perisylvian language areas. On the other hand, operations that are typically solved by procedural strategies, such as subtractions, rely on the manipulation of quantity representations, located in the IPS and superior parietal lobe. The observed association between the arcuate fasciculus-anterior and addition/multiplication is consistent with this because the parietal projections of the arcuate fasciculus-anterior found by tractography (for a summary see Catani et al., 2005) terminate in inferior parietal areas and posterior temporal areas (encompassing BA 22, 37, 39, and 40), which have been implicated in arithmetic fact retrieval (e.g., Delazer et al., 2003; Grabner et al., 2009; Prado et al., 2011). On the other hand, arcuate fasciculus fibers do not reach the superior parietal lobe, which might explain why we did not observe a significant association between the arcuate fasciculus-anterior and subtraction/division. The current findings of neural dissociation among arithmetic operations coincide with the results of several functional neuroimaging studies showing that neural networks involved in arithmetic problem solving differ between arithmetic operation and strategy use (e.g., Fehr et al., 2007; Grabner et al., 2009; Prado et al., 2011; Zhou et al., 2007). They also concur with Event Related Potentials data (Zhou et al., 2006), which showed neural dissociation among addition, subtraction, and multiplication. Compared to addition and subtraction, single-digit multiplication elicited a greater N300 at the left frontal electrodes, which was interpreted as a greater dependence on verbal processing (in the left frontal region) for the retrieval of simple multiplication facts compared to subtraction.

Fifth, we also explored how the observed associations between the left arcuate fasciculus-anterior and addition/multiplication might be explained by different types of reading ability. Such data might further shed light on the association between reading and arithmetic (e.g., Simmons and Singleton, 2008). A reasonable explanation on why the left arcuate fasciculus seems more important for addition and multiplication as opposed to subtraction and division may lie in the neural overlap between reading and these two arithmetic operations. More specifically, in reading, it is well demonstrated that phonological representations are necessary in order to learn to read an alphabetic script, and that such representations are important during the initial stages of reading and the reading of non-familiar words, such as non-words (e.g. Hulme, 2002). In arithmetic, phonological representations might be particularly important for retrieval of existing arithmetic facts, which might be stored in a phonological code in long-term memory (e.g. De Smedt et al., 2010; Simmons and Singleton, 2008). Reading studies have provided evidence for the role of the left arcuate fasciculus in phonological processing during speech perception and production (e.g., Vandermosten et al., 2012a; Yeatman et al., 2011; see for a review Dick and Tremblay, 2012). The correlation analyses with measures of reading ability taken into account showed that phonological decoding rather than orthographic decoding does account for the observed relationship between addition/multiplication and FA in the left arcuate fasciculus-anterior. This suggests that the association between the arcuate fasciculus and addition/multiplication might reflect a common reliance on phonological processing. It is likely that the brain uses the arcuate fasciculus-anterior for solving addition and multiplication because the signals carried within the arcuate fasciculus are used for the manipulation of phonological information. These findings are in line with neuroimaging studies which have shown neural overlap in the left temporo-parietal cortex between arithmetic and reading, more specifically during reading of non-words, and at the initial stages of reading development (Dehaene et al., 2003; Pugh et al., 2001; Simmons and Singleton, 2008).

Finally, it is important to note that the observed relationship between fractional anisotropy in the left arcuate fasciculus-anterior and arithmetic does not generalize to the right hemisphere or adjacent white matter tracts in the fronto-temporo-parietal region commonly active during arithmetic tasks. Thus, the observed relationship between white matter and arithmetic fact retrieval is specifically localized to the left anterior part of the arcuate fasciculus (which connects frontal and inferior parietal areas in the brain). In accordance with Tsang et al. (2009), this clearly shows the anatomical specificity of the arithmetic correlation found in the fronto-parietal area.

5. Conclusions

Research about the neural correlates underlying arithmetic processing has undergone rapid progress in recent years. Functional neuroimaging has shown that arithmetic activates a fronto-parietal network (Arsalidou and Taylor, 2011) and that activity in this network is modulated by operation and individual differences (De Smedt et al., 2011; Grabner et al., 2007, 2009). Extending the existing body of data with DTI tractography data, our findings show a link between arithmetic and the white matter structure that connects regions of the fronto-parietal arithmetic network and that this is modulated by operation and individual differences. More specifically, fractional anisotropy of the left arcuate fasciculus-anterior correlates with individual differences in addition and multiplication, but not with subtraction and division in healthy 12-year-old children. Our findings have implications for understanding the underlying neurobiological mechanisms of individual differences in arithmetical competence. Future DTI studies should investigate whether training for addition and multiplication may influence structural connectivity in the fronto-parietal arithmetic network. In addition, the role of phonological processing in addition/multiplication needs to be further explored at behavioral and neuroimaging levels.

Acknowledgements

This research was supported by the “Research Foundation Flanders” FWO (grant number G.0359.10). We thank the children and their families for their time and contribution to this study.

References

Ansari, D., Garcia, N., Lucas, E., Hamon, K., & Dhital, B. (2005). Neural correlates of symbolic number processing in children and adults. *Neuroreport, 16*(16), 1769-1773. http://dx.doi.org/10.1097/01.wnr.0000183905.23396.f1

Ansari, D. (2008). Effects of development and enculturation on number representation in the brain. *Nature Reviews Neuroscience, 9*(4), 278-291. http://dx.doi.org/10.1038/nrn2334

Ansari, D., & Dhital, B. (2006). Age-related changes in the activation of the intraparietal sulcus during nonsymbolic magnitude processing: An event-related functional magnetic resonance imaging study. *Journal of Cognitive Neuroscience, 18*(11), 1820-1828. http://dx.doi.org/10.1162/jocn.2006.18.11.1820

Arsalidou, M., & Taylor, M. J. (2011). Is 2+2=4? Meta-analyses of brain areas needed for numbers and calculations. *NeuroImage, 54*(3), 2382-2393. http://dx.doi.org/10.1016/j.neuroimage.2010.10.009

Ashkenazi, S., Black, J. M., Abrams, D. A., Hoeft, F., & Menon, V. (2013). Neurobiological Underpinnings of Math and Reading Learning Disabilities. *Journal of Learning Disabilities*. http://dx.doi.org/10.1177/0022219413483174

Barnea-Goraly, N., Eliez, S., Menon, V., Bammer, R., & Reiss, A. L. (2005). Arithmetic ability and parietal alterations: A diffusion tensor imaging study in Velocardiofacial syndrome. *Cognitive Brain Research, 25*(3), 735-740. http://dx.doi.org/10.1016/j.cogbrainres.2005.09.013

Barrouillet, P., Mignon, M., & Thevenot, C. (2008). Strategies in subtraction problem solving in children. *Journal of Experimental Child Psychology, 99*(4), 233-251. http://dx.doi.org/10.1016/j.jecp.2007.12.001

Basser, P. J., Mattiello, J., & Lebihan, D. (1994). MR Diffusion Tensor Spectroscopy and Imaging. *Biophysical Journal, 66*(1), 259-267.

Beaulieu, C. (2002). The basis of anisotropic water diffusion in the nervous system - a technical review. *Nmr in Biomedicine, 15*(7-8), 435-455. http://dx.doi.org/10.1002/nbm.782

Beaulieu, C., Plewes, C., Paulson, L. A., Roy, D., Snook, L., Concha, L., & Phillips, L. (2005). Imaging brain connectivity in children with diverse reading ability. *NeuroImage, 25*(4), 1266-1271. http://dx.doi.org/10.1016/j.neuroimage.2004.12.053

Brus, B. T., & Voeten, M. J. M. (1979). *Een-Minuut-Test. Vorm A en B. Schoolvorderingentest voor de technische leesvaardigheid, bestemd voor groep 4 tot en met 8 van het basisonderwijs. Verantwoording en Handleiding.* Nijmegen: Berkhout.

Campbell, J. I. D., & Xue, Q. L. (2001). Cognitive arithmetic across cultures. *Journal of Experimental Psychology-General, 130*(2), 299-315. http://dx.doi.org/10.1037//0096-3445.130.2.299

Cantlon, J. F., Brannon, E. M., Carter, E. J., & Pelphrey, K. A. (2006). Functional imaging of numerical processing in adults and 4-y-old children. *Plos Biology, 4*(5), 844-854. http://dx.doi.org/10.1371/journal.pbio.0040125

Catani, M., Allin, M. P. G., Husain, M., Pugliese, L., Mesulam, M. M., Murray, R. M., & Jones, D. K. (2007). Symmetries in human brain language pathways correlate with verbal recall. *Proceedings of the National Academy of Sciences of the United States of America, 104*(43), 17163-17168. http://dx.doi.org/10.1073/pnas.0702116104

Catani, M., Jones, D. K., & Ffytche, D. H. (2005). Perisylvian language networks of the human brain. *Annals of Neurology, 57*(1), 8-16. http://dx.doi.org/10.1002/ana.20319
Catani, M., & Thiebaut de Schotten, M. (2008). A diffusion tensor imaging tractography atlas for virtual in vivo dissections. *Cortex, 44*(8), 1105-1132. http://dx.doi.org/10.1016/j.cortex.2008.05.004
Cercignani, M. (2010). Strategies for patient-control comparison of diffusion MR data. In D. K. Jones (Ed.), *Diffusion MRI: Theory, Methods and Applications* (pp. 485-499). Oxford: Oxford University Press.
Cho, S., Metcalfe, A. W. S., Young, C. B., Ryali, S., Geary, D. C., & Menon, V. (2012). Hippocampal-Prefrontal Engagement and Dynamic Causal Interactions in the Maturation of Children's Fact Retrieval. *Journal of Cognitive Neuroscience, 24*(9), 1849-1866.
Cho, S., Ryali, S., Geary, D. C., & Menon, V. (2011). How does a child solve 7+8? Decoding brain activity patterns associated with counting and retrieval strategies. *Developmental Science, 14*(5), 989-1001. http://dx.doi.org/10.1111/j.1467-7687.2011.01055.x
Chochon, F., Cohen, L., van de Moortele, P. F., & Dehaene, S. (1999). Differential contributions of the left and right inferior parietal lobules to number processing. *Journal of Cognitive Neuroscience, 11*(6), 617-630. http://dx.doi.org/10.1162/089892999563689
Christoff, K., & Gabrieli, J. D. E. (2000). The frontopolar cortex and human cognition: Evidence for a rostrocaudal hierarchical organization within the human prefrontal cortex. *Psychobiology, 28*(2), 168-186.
Cohen, L., Dehaene, S., Chochon, F., Lehericy, S., & Naccache, L. (2000). Language and calculation within the parietal lobe: a combined cognitive, anatomical and fMRI study. *Neuropsychologia, 38*(10), 1426-1440. http://dx.doi.org/10.1016/s0028-3932(00)00038-5
Cohen, L., Dehaene, S., Vinckier, F., Jobert, A., & Montavont, A. (2008). Reading normal and degraded words: Contribution of the dorsal and ventral visual pathways. *NeuroImage, 40*(1), 353-366. http://dx.doi.org/10.1016/j.neuroimage.2007.11.036
Davis, N., Cannistraci, C. J., Rogers, B. P., Gatenby, J. C., Fuchs, L. S., Anderson, A. W., & Gore, J. C. (2009). The neural correlates of calculation ability in children: an fMRI study. *Magnetic Resonance Imaging, 27*(9), 1187-1197. http://dx.doi.org/10.1016/j.mri.2009.05.010
Deprez, S., Amant, F., Smeets, A., Peeters, R., Leemans, A., Van Hecke, W., . . . Sunaert, S. (2012). Longitudinal Assessment of Chemotherapy-Induced Structural Changes in Cerebral White Matter and Its Correlation With Impaired Cognitive Functioning. *Journal of Clinical Oncology*, *30*(3), 274-281. http://dx.doi.org/10.1200/jco.2011.36.8571
De Smedt, B., Holloway, I. D., & Ansari, D. (2011). Effects of problem size and arithmetic operation on brain activation during calculation in children with varying levels of arithmetical fluency. *NeuroImage, 57*(3), 771-781. http://dx.doi.org/10.1016/j.neuroimage.2010.12.037
De Smedt, B., Janssen, R., Bouwens, K., Verschaffel, L., Boets, B., & Ghesquiere, P. (2009). Working memory and individual differences in mathematics achievement: A longitudinal study from first grade to second grade. *Journal of Experimental Child Psychology, 103*(2), 186-201. http://dx.doi.org/10.1016/j.jecp.2009.01.004
De Smedt, B., Taylor, J., Archibald, L., & Ansari, D. (2010). How is phonological processing related to individual differences in children's arithmetic skills? *Developmental Science, 13*(3), 508-520. http://dx.doi.org/10.1111/j.1467-7687.2009.00897.x
De Vos, T. (1992). *Tempo Test Rekenen (TTR)*. Nijmegen: Berkhout.
Dehaene, S. (1992). Varieties of numerical abilities. *Cognition, 44*(1-2), 1-42. http://dx.doi.org/10.1016/0010-0277(92)90049-n
Dehaene, S., & Cohen, L. (1997). Cerebral pathways for calculation: Double dissociation between rote verbal and quantitative knowledge of arithmetic. *Cortex, 33*(2), 219-250. http://dx.doi.org/10.1016/s0010-9452(08)70002-9
Dehaene, S., Piazza, M., Pinel, P., & Cohen, L. (2003). Three parietal circuits for number processing. *Cognitive Neuropsychology, 20*(3-6), 487-506. http://dx.doi.org/10.1080/02643290244000239
Delazer, M., Domahs, F., Bartha, L., Brenneis, C., Lochy, A., Trieb, T., & Benke, T. (2003). Learning complex arithmetic - an fMRI study. *Cognitive Brain Research, 18*(1), 76-88. http://dx.doi.org/10.1016/j.cogbraines.2003.09.005

Delazer, M., Ischebeck, A., Domahs, F., Zamarian, L., Koppelstaetter, F., Siedentopf, C. M., . . . Felber, S. (2005). Learning by strategies and learning by drill - evidence from an fMRI study. *NeuroImage, 25*(3), 838-849. http://dx.doi.org/10.1016/j.neuroimage.2004.12.009

Dick, A. S., & Tremblay, P. (2012). Beyond the arcuate fasciculus: consensus and controversy in the connectional anatomy of language. *Brain, 135*, 3529-3550. http://dx.doi.org/10.1093/brain/aws222

Dowker, A. (2005). Early identification and inteirvention for students with mathematics difficulties. *Journal of Learning Disabilities, 38*(4), 324-332. http://dx.doi.org/10.1177/00222194050380040801

Fehr, T., Code, C., & Herrmann, M. (2007). Common brain regions underlying different arithmetic operations as revealed by conjunct fMRI-BOLD activation. *Brain Research, 1172*, 93-102. http://dx.doi.org/10.1016/j.brainres.2007.07.043

Gathercole, S. E., Pickering, S. J., Ambridge, B., & Wearing, H. (2004). The structure of working memory from 4 to 15 years of age. *Developmental Psychology, 40*(2), 177-190. http://dx.doi.org/10.1037/0012-1649.40.2.177

Geary, D. C. (2004). Mathematics and learning disabilities. *Journal of Learning Disabilities, 37*(1), 4-15. http://dx.doi.org/10.1177/00222194040370010201

Geary, D. C. (2010). Mathematical disabilities: Reflections on cognitive, neuropsychological, and genetic components. *Learning and Individual Differences, 20*(2), 130-133. http://dx.doi.org/10.1016/j.lindif.2009.10.008

Goswami, U., & Szucs, D. (2011). Educational neuroscience: Developmental mechanisms: Towards a conceptual framework. *NeuroImage, 57*(3), 651-658. http://dx.doi.org/10.1016/j.neuroimage.2010.08.072

Grabner, R. H., Ansari, D., Koschutnig, K., Reishofer, G., Ebner, F., & Neuper, C. (2009). To retrieve or to calculate? Left angular gyrus mediates the retrieval of arithmetic facts during problem solving. *Neuropsychologia, 47*(2), 604-608. http://dx.doi.org/10.1016/j.neuropsychologia.2008.10.013

Grabner, R. H., Ansari, D., Reishofer, G., Stern, E., Ebner, F., & Neuper, C. (2007). Individual differences in mathematical competence predict parietal brain activation during mental calculation. *NeuroImage, 38*(2), 346-356. http://dx.doi.org/10.1016/j.neuroimage.2007.07.041

Hulme, C. (2002). Phonemes, rimes, and the mechanisms of early reading development. [Editorial Material]. *Journal of Experimental Child Psychology, 82*(1), 58-64. http://dx.doi.org/10.1006/jecp.2002.2674

Imbo, I., & Vandierendonck, A. (2008). Effects of problem size, operation, and working-memory span on simple-arithmetic strategies: differences between children and adults? *Psychological Research-Psychologische Forschung, 72*(3), 331-346. http://dx.doi.org/10.1007/s00426-007-0112-8

Ischebeck, A., Zamarian, L., Egger, K., Schocke, M., & Delazer, M. (2007). Imaging early practice effects in arithmetic. *NeuroImage, 36*(3), 993-1003. http://dx.doi.org/10.1016/j.neuroimage.2007.03.051

Ischebeck, A., Zamarian, L., Schocke, M., & Delazer, M. (2009). Flexible transfer of knowledge in mental arithmetic - An fMRI study. *NeuroImage, 44*(3), 1103-1112. http://dx.doi.org/10.1016/j.neuroimage.2008.10.025

Ischebeck, A., Zamarian, L., Siedentopf, C., Koppelstatter, F., Benke, T., Felber, S., & Delazer, M. (2006). How specifically do we learn? Imaging the learning of multiplication and subtraction. *NeuroImage, 30*(4), 1365-1375. http://dx.doi.org/10.1016/j.neuroimage.2005.11.016

Jobard, G., Crivello, F., & Tzourio-Mazoyer, N. (2003). Evaluation of the dual route theory of reading: a metanalysis of 35 neuroimaging studies. *NeuroImage, 20*(2), 693-712. http://dx.doi.org/10.1016/s1053-8119(03)00343-4

Jones, D. K. (2008). Studying connections in the living human brain with diffusion MRI. *Cortex, 44*(8), 936-952. http://dx.doi.org/10.1016/j.cortex.2008.05.002

Jordan, N. C., Hanich, L. B., & Kaplan, D. (2003). Arithmetic fact mastery in young children: A longitudinal investigation. *Journal of Experimental Child Psychology, 85*(2), 103-119. http://dx.doi.org/10.1016/s0022-0965(03)00032-8

Jost, K., Khader, P., Burke, M., Bien, S., & Rosler, F. (2009). Dissociating the solution processes of small, large, and zero multiplications by means of fMRI. *NeuroImage, 46*(1), 308-318. http://dx.doi.org/10.1016/j.neuroimage.2009.01.044

Kaufmann, L., Wood, G., Rubinsten, O., & Henik, A. (2011). Meta-Analyses of Developmental fMRI Studies Investigating Typical and Atypical Trajectories of Number Processing and Calculation. *Developmental Neuropsychology, 36*(6), 763-787. http://dx.doi.org/10.1080/87565641.2010.549884

Kawashima, R., Taira, M., Okita, K., Inoue, K., Tajima, N., Yoshida, H., . . . Fukuda, H. (2004). A functional MRI study of simple arithmetic - a comparison between children and adults. *Cognitive Brain Research, 18*(3), 227-233. http://dx.doi.org/10.1016/j.cogbrainres.2003.10.009

Kazui, H., Kitagaki, H., & Mori, E. (2000). Cortical activation during retrieval of arithmetical facts and actual calculation: A functional magnetic resonance imaging study. *Psychiatry and Clinical Neurosciences, 54*(4), 479-485. http://dx.doi.org/10.1046/j.1440-1819.2000.00739.x

Kilpatrick, J., Swafford, J., & Findell, B. (2001). *Adding it up: Helping children learn mathematics*. Washington, DC: National Academies Press.

Kort, W., Schittekatte, M., Dekker, P. H., Verhaeghe, P., Compaan, E. L., Bosmans, M., & Vermeir, G. (2005). *WISC-III NL Wechsler Intelligence Scale for Children. Derde Editie NL. Handleiding en Verantwoording*. Amsterdam: Harcourt Test Publishers/Nederlands Instituut voor Psychologen.

Kucian, K., von Aster, M., Loenneker, T., Dietrich, T., & Martin, E. (2008). Development of neural networks for exact and approximate calculation: A fMRI study. *Developmental Neuropsychology, 33*(4), 447-473. http://dx.doi.org/10.1080/87565640802101474

Le Bihan, D., Mangin, J. F., Poupon, C., Clark, C. A., Pappata, S., Molko, N., & Chabriat, H. (2001). Diffusion tensor imaging: Concepts and applications. *Journal of Magnetic Resonance Imaging, 13*(4), 534-546. http://dx.doi.org/10.1002/jmri.1076

Lebel, C., Rasmussen, C., Wyper, K., Andrew, G., & Beaulieu, C. (2010). Brain Microstructure Is Related to Math Ability in Children With Fetal Alcohol Spectrum Disorder. *Alcoholism-Clinical and Experimental Research, 34*(2), 354-363. http://dx.doi.org/10.1111/j.1530-0277.2009.01097.x

Lee, K. M. (2000). Cortical areas differentially involved in multiplication and subtraction: A functional magnetic resonance imaging study and correlation with a case of selective acalculia. *Annals of Neurology, 48*(4), 657-661. http://dx.doi.org/10.1002/1531-8249(200010)48:4<657::aid-ana13>3.0.co;2-k

Leemans, A., Jeurissen, B., Sijbers, J., & Jones, D.K. (2009). ExploreDTI: A graphical toolbox for processing, analyzing, and visualizing diffusion MR data. In 17th Annual Meeting of International Society for Magnetic Resonance in Medicine, Hawaii, USA, 3537.

Matejko, A. A., Price, G. R., Mazzocco, M. M. M., & Ansari, D. (2013). Individual differences in left parietal white matter predict math scores on the Preliminary Scholastic Aptitude Test. *NeuroImage, 66*(0), 604-610. http://dx.doi.org/http://dx.doi.org/10.1016/j.neuroimage.2012.10.045

Meintjes, E. M., Jacobson, S. W., Molteno, C. D., Gatenby, J. C., Warton, C., Cannistraci, C. J., . . . Jacobson, J. L. (2010). An fMRI study of magnitude comparison and exact addition in children. *Magnetic Resonance Imaging, 28*(3), 351-362. http://dx.doi.org/10.1016/j.mri.2009.11.010

Menon, V., Rivera, S. M., White, C. D., Eliez, S., Glover, G. H., & Reiss, A. L. (2000a). Functional optimization of arithmetic processing in perfect performers. *Cognitive Brain Research, 9*(3), 343-345. http://dx.doi.org/10.1016/s0926-6410(00)00010-0

Menon, V., Rivera, S. M., White, C. D., Glover, G. H., & Reiss, A. L. (2000b). Dissociating prefrontal and parietal cortex activation during arithmetic processing. *NeuroImage, 12*(4), 357-365. http://dx.doi.org/10.1006/nimg.2000.0613

Mori, S. (2007). *Introduction to Diffusion Tensor Imaging*. Amsterdam: Elsevier.

Mukherjee, P., Chung, S. W., Berman, J. I., Hess, C. P., & Henry, R. G. (2008). Diffusion tensor MR imaging and fiber tractography: Technical considerations. *American Journal of Neuroradiology, 29*(5), 843-852. http://dx.doi.org/10.3174/ajnr.A1052

Nagy, Z., Westerberg, H., & Klingberg, T. (2004). Maturation of white matter is associated with the development of cognitive functions during childhood. [Article]. *Journal of Cognitive Neuroscience, 16*(7), 1227-1233. http://dx.doi.org/10.1162/0898929041920441

Oishi, K., Faria, A.V., Zijl, P.C.M.V., Mori, S. (2011). *MRI Atlas of Human White Matter* (2nd ed.). London: Academic Press.

Oldfield, R. C. (1971). The Assessment and Analysis of Handedness: the Edinburgh Inventory. *Neuropsychologia, 9*(1), 97-113. http://dx.doi.org/10.1016/0028-3932(71)90067-4

Olesen, P. J., Nagy, Z., Westerberg, H., & Klingberg, T. (2003). Combined analysis of DTI and fMRI data reveals a joint maturation of white and grey matter in a fronto-parietal network. *Cognitive Brain Research, 18*(1), 48-57. http://dx.doi.org/10.1016/j.cogbrainres.2003.09.003

Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-back working memory paradigm: A meta-analysis of normative functional neuroimaging. *Human Brain Mapping, 25*(1), 46-59. http://dx.doi.org/10.1002/hbm.20131

Piazza, M., Pinel, P., Le Bihan, D., & Dehaene, S. (2007). A magnitude code common to numerosities and number symbols in human intraparietal cortex. *Neuron, 53*(2), 293-305. http://dx.doi.org/10.1016/j.neuron.2006.11.022

Pickering, S. J., & Gathercole, S. E. (2001). *Working memory battery for children*. London: Psychological Corporation UK.

Prado, J., Mutreja, R., Zhang, H. C., Mehta, R., Desroches, A. S., Minas, J. E., & Booth, J. R. (2011). Distinct Representations of Subtraction and Multiplication in the Neural Systems for Numerosity and Language. *Human Brain Mapping, 32*(11), 1932-1947. http://dx.doi.org/10.1002/hbm.21159

Pugh, K. R., Mencl, W. E., Jenner, A. R., Katz, L., Frost, S. J., Lee, J. R., . . . Shaywitz, B. A. (2000). Functional neuroimaging studies of reading and reading disability (developmental dyslexia). *Mental Retardation and Developmental Disabilities Research Reviews, 6*(3), 207-213. http://dx.doi.org/10.1002/1098-2779(2000)6:3<207::aid-mrdd8>3.0.co;2-p

Pugh, K. R., Mencl, W. E., Jenner, A. R., Katz, L., Frost, S. J., Lee, J. R., . . . Shaywitz, B. A. (2001). Neurobiological studies of reading and reading disability. *Journal of Communication Disorders, 34*(6), 479-492. http://dx.doi.org/10.1016/s0021-9924(01)00060-0

Rickard, T. C., Romero, S. G., Basso, G., Wharton, C., Flitman, S., & Grafman, J. (2000). The calculating brain: an fMRI study. *Neuropsychologia, 38*(3), 325-335. http://dx.doi.org/10.1016/s0028-3932(99)00068-8

Rivera, S. M., Reiss, A. L., Eckert, M. A., & Menon, V. (2005). Developmental changes in mental arithmetic: Evidence for increased functional specialization in the left inferior parietal cortex. *Cerebral Cortex, 15*(11), 1779-1790. http://dx.doi.org/10.1093/cercor/bhi055

Rosenberg-Lee, M., Barth, M., & Menon, V. (2011). What difference does a year of schooling make? Maturation of brain response and connectivity between 2nd and 3rd grades during arithmetic problem solving. *NeuroImage, 57*(3), 796-808. http://dx.doi.org/10.1016/j.neuroimage.2011.05.013

Rykhlevskaia, E., Uddin, L. Q., Kondos, L., & Menon, V. (2009). Neuroanatomical correlates of developmental dyscalculia: combined evidence from morphometry and tractography. *Frontiers in Human Neuroscience, 3*. http://dx.doi.org/10.3389/neuro.09.051.2009

Sandak, R., Mencl, W. E., Frost, S. J., & Pugh, K. R. (2004). The neurobiological basis of skilled and impaired reading: Recent findings and new directions. *Scientific Studies of Reading, 8*(3), 273-292. http://dx.doi.org/10.1207/s1532799xssr0803_6

Sattler, J. M. (2001). *Assessment of children : Cognitive applications* (4th ed.). San Diego: Jerome M. Sattler Publisher, Inc.

Schlaggar, B. L., & McCandliss, B. D. (2007). Development of neural systems for reading *Annual Review of Neuroscience* (Vol. 30, pp. 475-503). Palo Alto: Annual Reviews.

Schmithorst, V. J., & Brown, R. D. (2004). Empirical validation of the triple-code model of numerical processing for complex math operations using functional MRI and group Independent Component Analysis of the mental addition and subtraction of fractions. *NeuroImage, 22*(3), 1414-1420. http://dx.doi.org/10.1016/j.neuroimage.2004.03.021

Schmithorst, V. J., Wilke, M., Dardzinski, B. J., & Holland, S. K. (2005). Cognitive functions correlate with white matter architecture in a normal pediatric population: A diffusion tensor MRI study. *Human Brain Mapping, 26*(2), 139-147. http://dx.doi.org/10.1002/hbm.20149

Siegler, R. S. (1996). *Emerging minds: The process of change in children's thinking*. New York: Oxford University Press.

Simmons, F. R., & Singleton, C. (2008). Do weak phonological representations impact on arithmetic development? A review of research into arithmetic and dyslexia. *Dyslexia, 14*(2), 77-94. http://dx.doi.org/10.1002/dys.341

Simon, O., Mangin, J. F., Cohen, L., Le Bihan, D., & Dehaene, S. (2002). Topographical layout of hand, eye, calculation, and language-related areas in the human parietal lobe. *Neuron, 33*(3), 475-487. http://dx.doi.org/10.1016/s0896-6273(02)00575-5

Simos, P. G., Breier, J. I., Fletcher, J. M., Foorman, B. R., Castillo, E. M., & Papanicolaou, A. C. (2002). Brain mechanisms for reading words and pseudowords: an integrated approach. *Cerebral Cortex, 12*(3), 297-305. http://dx.doi.org/10.1093/cercor/12.3.297

Till, C., Deotto, A., Tipu, V., Sled, J. G., Bethune, A., Narayanan, S., . . . Banwell, B. L. (2011). White matter integrity and math performance in pediatric multiple sclerosis: a diffusion tensor imaging study. *Neuroreport, 22*(18), 1005-1009. http://dx.doi.org/10.1097/WNR.0b013e32834dc301

Tsang, J. M., Dougherty, R. F., Deutsch, G. K., Wandell, B. A., & Ben-Shachar, M. (2009). Frontoparietal white matter diffusion properties predict mental arithmetic skills in children. *Proceedings of the National Academy of Sciences of the United States of America, 106*(52), 22546-22551. http://dx.doi.org/10.1073/pnas.0906094106

van Eimeren, L., Grabner, R. H., Koschutnig, K., Reishofer, G., Ebner, F., & Ansari, D. (2010). Structure-function relationships underlying calculation: A combined diffusion tensor imaging and fMRI study. *NeuroImage, 52*(1), 358-363. http://dx.doi.org/10.1016/j.neuroimage.2010.04.001

van Eimeren, L., Niogi, S. N., McCandliss, B. D., Holloway, I. D., & Ansari, D. (2008). White matter microstructures underlying mathematical abilities in children. *Neuroreport, 19*(11), 1117-1121.

van den Bos, K. P., Spelberg, H. C. L., Scheepstra, A. J. M., & De Vries, J. R. (1994). *De Klepel. Vorm A en B. Een Test Voor de Leesvaardigheid Van Pseudowoorden. Verantwoording, Handleiding, Diagnostiek en Behandeling [Word and Nonword Reading Test A and B manual]*. Nijmegen: Berkhout.

Vandermosten, M., Boets, B., Poelmans, H., Sunaert, S., Wouters, J., & Ghesquiere, P. (2012a). A tractography study in dyslexia: neuroanatomic correlates of orthographic, phonological and speech processing. *Brain, 135*, 935-948. http://dx.doi.org/10.1093/brain/awr363

Vandermosten, M., Boets, B., Wouters, J., & Ghesquiere, P. (2012b). A qualitative and quantitative review of diffusion tensor imaging studies in reading and dyslexia. *Neuroscience and Biobehavioral Reviews, 36*(6), 1532-1552. http://dx.doi.org/10.1016/j.neubiorev.2012.04.002

Wakana, S., Caprihan, A., Panzenboeck, M. M., Fallon, J. H., Perry, M., Gollub, R. L., . . . Mori, S. (2007). Reproducibility of quantitative tractography methods applied to cerebral white matter. *NeuroImage, 36*(3), 630-644. http://dx.doi.org/10.1016/j.neuroimage.2007.02.049

Wang, R., & Wedeen, V.J. (2007). TrackVis.org, Martinos Center for Biomedical Imaging, Massachusetts General Hospital. ISMRM abstract Proceedings International Society for Magnetic Resonance in Medicine, 15, 3720.

Yeatman, J. D., Dougherty, R. F., Rykhlevskaia, E., Sherbondy, A. J., Deutsch, G. K., Wandell, B. A., & Ben-Shachar, M. (2011). Anatomical Properties of the Arcuate Fasciculus Predict Phonological and Reading Skills in Children. *Journal of Cognitive Neuroscience, 23*(11), 3304-3317.

Zamarian, L., Ischebeck, A., & Delazer, M. (2009). Neuroscience of learning arithmetic-Evidence from brain imaging studies. *Neuroscience and Biobehavioral Reviews, 33*(6), 909-925. http://dx.doi.org/10.1016/j.neubiorev.2009.03.005

Zhou, X., Chen, C., Dong, Q., Zhang, H., Zhou, R., Zhao, H., . . . Guo, Y. (2006). Event-related potentials of single-digit addition, subtraction, and multiplication. *Neuropsychologia, 44*(12), 2500-2507. http://dx.doi.org/10.1016/j.neuropsychologia.2006.04.003

Zhou, X. L., Chen, C. S., Zang, Y. F., Dong, Q., Chen, C. H., Qiao, S. B., & Gong, Q. Y. (2007). Dissociated brain organization for single-digit addition and multiplication. *NeuroImage*, *35*(2), 871-880. http://dx.doi.org/10.1016/j.neuroimage.2006.12.017